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With the author

ON THE ACTION
OF THE
HYDRATED SESQUIOXIDE OF IRON ON ARSENIC.

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The hydrated sesquioxide of iron was first proposed as an antidote for arsenic by Drs Bunsen and Berthold of Gottingen, who published a pamphlet on the subject in Germany. The importance of the question led many experimenters, especially on the continent, to put its powers fairly to the test, and there seems little reason to doubt that when administered in sufficient quantity, it either arrests or totally prevents the action of the poison on animals. The following experiments were instituted with a view to throw some light on the *modus operandi* of the antidote, by investigating the chemical action of the hydrated oxide on arsenic. I considered it unnecessary to sacrifice any more animals to experiments with arsenic, as the numerous trials of this kind that have been already made, and which have been collected by Dr Donald Mackenzie in his probationary essay on the Antidotes to Arsenic, appear to me to be quite satisfactory. In this country the efficacy of the oxide of iron as an antidote, and its power of combining with arsenic have been called in question by Messrs Brett* and Orton.† But with respect to the former, it may be observed, that he appears uniformly to have used too small quantities of the oxide; and the experiments of the latter hardly seem to have been made with sufficient care, as appears in one instance, at least, from his having injected both poison and antidote into the lungs instead of the stomach of the rabbit.*

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* Medical Gazette, 1834-35, p. 220.

† Lancet, 1834-35, p. 232.

It has been supposed by some that the oxide may prove preventive of the action of the arsenic mechanically, as charcoal has been found to do, by enveloping the poison, and protecting the stomach from its contact, and the large quantity in which the oxide requires to be employed, naturally favours such a supposition. It has been found, however, that the hydrated sesquioxide of iron has the power of removing arsenic from its solutions in water, and from this we are led to infer that it has really the power of combining with the poison, and rendering it insoluble. In order to remove the arsenic totally, a large amount of oxide requires to be employed. Mr Brett did not succeed in doing so when he used eight or ten grains of oxide to one of arsenic; but Dr Mackenzie removed arsenic completely from its solution, when he used the proportion of twelve grains of oxide to one of arsenic.

The following experiments will show the results which I have obtained from parallel trials.

Expt. I. One grain of arsenious acid dissolved in water was, when cold, agitated for a few minutes with a quantity of the magma equal to about four grains of dry oxide, filtered and tested. The fluid was found to indicate arsenic distinctly on applying the usual tests. The remainder of the solution was retained on the ferrugo, and left in contact for eighteen hours, when it was found that the arsenic was completely removed.

On repeating this experiment several times, the result was not always the same. In all the instances, traces, more or less distinct, of arsenic, were detected in the filtered fluid; but I did not always succeed in completely removing the arsenic, by leaving them in contact for eighteen hours. These variations were probably owing to some portions of the magma being less completely expressed than others, and therefore containing in a given weight a smaller amount of oxide.

These trials agree in a great measure with the experiments of

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* The hydrated sesquioxide has been introduced into the New Edinburgh Pharmacopœia under the name of Ferrugo, and is prepared by dissolving sulphate of iron in water with a little sulphuric acid, adding nitric acid by degrees till it is thus fully oxygenated, and then precipitating the hydrated sesquioxide from this solution by an excess of ammonia. The product thus obtained is of a deep reddish brown. If dried cautiously at a temperature not exceeding 180°, it retains according to the Pharmacopœia, about 18 per cent. of water, and it is likewise found that, however well it may be washed, it still retains a small proportion of ammonia, which may be driven off by further exposure to heat. It is found to answer best as an antidote when kept in the moist state, being then in the finest possible state of division. That which I used in the following experiments had been expressed after washing, and contained in 100 grains of the mass a quantity equivalent to 20 grains of the oxide dried at 180°.

Mr Brett. It was obvious that the whole of the arsenic could not be removed by this amount of oxide; but it was equally evident that a considerable proportion of it had disappeared, for on comparing the amount of precipitate produced in the filtered liquid by sulphuretted hydrogen, with that obtained by the same reagent in an equal bulk of water containing about a tenth of a grain of arsenic, the latter had always a much deeper yellow colour.

I found likewise, like Mr Brett, that when these proportions had been employed, the oxide retained on the filter, after being washed free of adhering arsenic by cold water, yielded it readily to that fluid when poured upon it at a boiling heat, and, moreover, that very little arsenic was removed from the solution, if it was used at a temperature of 98°, and that a large amount reappeared in the fluid, if it was returned upon the ferrugo, and retained some time at that temperature.

The proportion of oxide of iron here was five times more than should have been required to saturate such an amount of arsenious acid, supposing them to form an arsenite of iron containing equal atoms of its constituents, yet it did not remove all the arsenic; and, moreover, what it had removed, was easily separated from it by water at the natural temperature of the stomach. Mr Brett was therefore not wrong in supposing that (in such proportion, at least,) the oxide could not be administered as an antidote to arsenic with any chance of success.

The result, however, was different when the oxide was employed in larger quantity.

Expt. II. One grain of arsenic dissolved in water was, when the fluid had cooled, agitated with a quantity of the magma containing twelve grains of the oxide. The filtered liquid in several different trials in no instance indicated more than a very indistinct trace of arsenic when tested with sulphuretted hydrogen, and generally it was found not to afford the slightest indications of its presence, and this occurred at a temperature of 98°, as well as in the cold.

The oxide retained on the filter, moreover, did not readily part with its arsenic to boiling water. When simply washed on the filter with boiling water, little or no arsenic was removed from it at all, and it appeared to retain it with so much force that it was with difficulty separated even when boiled for half an hour in a very large bulk of water. It thus appears that when in large quantity, the hydrated oxide of iron has the power of removing arsenic completely from its solution in water, and that it retains the arsenic with such force as to render it *à priori* probable that it should from its insoluble condition be rendered inert.

Expt. III. The oxide carefully dried at 180° was likewise tried, and was found to withdraw arsenic completely from its solution.

Sixty grains of this dry oxide were found to remove completely one grain of arsenic, but it was obviously very inferior in power to what it had been when in the form of magma, for twelve grains of the dry oxide appeared to produce little or no diminution in the quantity of arsenic in solution, twenty-four grains even when left in contact for half an hour had not removed any considerable quantity, and it was not until thirty-six grains of the oxide had been used and left in contact for half an hour, that any very marked removal of the arsenic appeared to have been obtained.

Expt. IV. Being anxious to ascertain whether the oxide of iron was capable of removing arsenic from its soluble combinations, as well as from its solution in water, half a grain of arsenic in the form of arsenite of potassa was agitated with a quantity of the magma equal to about eight grains of the dry oxide. On applying the sulphuretted hydrogen test to the filtered fluid it gave a very indistinct trace of yellow. For comparison, one drop of a solution of arsenite of potassa, equal to only the sixtieth of a grain of arsenic, was tested in an equal bulk of water, and gave a much deeper yellow tinge. It thus appears that the oxide of iron has the power not only of removing arsenic from its solution in water, but also of decomposing arsenites,—an effect which must be considered to be due to a real chemical combination of the oxide of iron with arsenious acid.

The oxide of iron thus appears capable of forming an insoluble, and, as appears from other experiments,* inert compound with arsenious acid. It is well known, however, that when arsenite of potassa and persulphate of iron are mixed an arsenite of iron is formed of very different qualities. This arsenite has a canary yellow colour, is soluble in acids and ammonia, and when treated with boiling water, as appears from Mr Brett's experiments, parts with a portion of its arsenic, and passes to a brick brown colour. This yellow arsenite, moreover, has been found to be highly poisonous. The brick brown matter left on the filter, even when hot water has ceased to act upon it, retains, as Mr Brett has shown, a proportion of arsenic. No attempt has been made to ascertain whether this last form of combination of arsenic and iron is poisonous, but the experiment might be of interest, as this brown substance, obtained by washing the yellow arsenite with boiling water, appears to retain the arsenic in a condition very similar to that in which it is placed when removed from its solution by a large quantity of the hydrated sesquioxide.

The presence of ammonia appears to have some effect in modifying the combinations of arsenious acid and iron. When the yellow arsenite of iron is dissolved in an acid and reprecipitated by the addition of aqua potassæ, it appears, as before, of its characteristic yellow colour; but when a similar solution in acid is neutralised by ammonia, the precipitate, instead of being yellow, has always a dirty brown colour. When this is connected with the fact that the oxide, when precipitated by ammonia, always retains a portion of that substance in spite of most careful washing, it leads to the supposition, that the presence of ammonia may be of some importance in determining the powers of the hydrated oxide as an antidote. Such seems to have been the opinion of Dr Bunsen, who administered a portion of ammonia along with the oxide; but this has been shown by other experimenters to be unnecessary. It has been supposed that the presence of ammonia in the oxide was essential, and that, therefore, the oxide, when intended for an antidote, should always be precipitated by that substance; but I find that even when precipitated by potash, the oxide still has the power, though in a very inferior degree, of removing arsenic from its solutions.

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* Lancet, 1834-5. British and Foreign Medical Review, Vol. i.

Expt. V. One grain of arsenic in solution was agitated with a quantity of moist oxide precipitated by potash, equal to 14 grains dry oxide. The fluid was found to retain distinct traces of arsenic; but when the amount of oxide was equal to 24 grains dry oxide, the arsenic was completely removed. This was equal to twice the amount required when the oxide had been prepared by ammonia and used moist, but much less than what was necessary when the dried ammoniacal oxide had been employed.

Having by these various experiments satisfied myself that the hydrated sesquioxide of iron in its different conditions has the power more or less of combining with arsenic and rendering it insoluble, I instituted a series of experiments to ascertain if possible with more precision in what proportions the oxide should be employed to remove the arsenic completely. For this purpose I prepared two solutions, the one of arsenite of potassa, the other of persulphate of iron, of such strengths that an equal bulk of each should contain respectively arsenious acid and sesquioxide of iron in atomic proportions. The solution of iron was purposely made with an excess of acid, in order that any yellow arsenite of iron which should be formed on mixing the solutions should be redissolved. The superabundant acid was then to be saturated by ammonia in excess, by which means I proposed to separate the oxide of iron in determinate proportion, and ascertain in what ratio it required to be employed, completely to remove the arsenic. The following results were obtained.

Expt. VI. When the solutions of arsenic and iron were mixed in the ratio of one proportion of each, the yellow arsenite was at once formed, but was immediately redissolved by the excess of acid. On adding ammonia in excess, a yellowish-brown precipitate was obtained, and the filtered fluid was pale orange. In this case, arsenite of iron had been thrown down, and again partially redissolved by the excess of ammonia. On boiling this solution the dissolved arsenite of iron was, on the expulsion of the ammonia, separated, and then by the boiling water decomposed, apparently in the same way in which the yellow arsenite is decomposed by washing with boiling water; a clear fluid being obtained containing arsenic, but no iron, and a dark-brown flocculent sediment being separated, still retaining a considerable proportion of arsenic.

Expt. VII. When the solutions of arsenic and iron were mixed in the ratio of two of the former to one of the latter, the yellow arsenite was at first formed, and immediately redissolved by the excess of acid. On adding ammonia in excess, the yellow precipitate reappeared, but was soon completely redissolved by excess of ammonia; the solution was of a dark orange colour, and was decomposed by boiling like the dissolved portion in last experiment; but with much greater difficulty, a large amount of iron remaining dissolved in the fluid for some time. Eventually, however, the whole of the iron was separated by boiling, and formed shining brown flakes, which retained likewise a large amount of arsenic.

Expt. VIII. When the solutions were mixed in the ratio of two of iron to one of arsenic, and ammonia added in excess, the precipitate obtained was of a dirty brown colour; the filtered fluid had a faint yellowish tinge, and obviously contained a small proportion of arsenite of iron dissolved by ammonia.*

Expt. IX. When three proportions of iron and one of arsenic were employed, and excess of ammonia added, the filtered fluid still contained arsenic distinctly, and a very faint trace of iron. The precipitate in external appearance resembled the ferrugo itself, and readily yielded a large amount of arsenic on washing it with boiling water.

Expt. X. The solutions of iron and arsenic were mixed in the proportions of four of the former to one of the latter, and ammonia added. The fluid separated by the filter was quite colourless; it contained distinct traces of arsenic, but no iron. The precipitate was like ferrugo in appearance, and yielded arsenic copiously on washing with warm water.

Expt. XI. Eight parts of the solution of iron to one of the arsenic were the proportions now mixed, and ammonia added. The filtered fluid contained an indistinct trace of arsenic, but no iron. The precipitate, which in external appearance resembled the last, gave no arsenic to cold water, and yielded it very sparingly to that fluid when boiling hot. Even by boiling it did not yield the arsenic so readily as the precipitate in Expt. X. did when merely washed with boiling water.

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* This solution gave a greenish-yellow tinge with sulphuretted hydrogen. When water contains yellow arsenite of iron suspended or dissolved in it, the colour struck by sulphuretted hydrogen is greenish-yellow, green, olive-green, or brownish-green, according to the amount of arsenite present.

Expt. XII. When the proportion of oxide of iron to the solution in arsenic was as twelve to one, and ammonia added, the filtered fluid was found to contain neither arsenic nor iron, and the precipitate yielded a bare trace of arsenic to warm water when poured on it.

From this last series of experiments, we learn that the state of combination of the oxide of iron and arsenious acid varies remarkably according to the relative proportions of these two substances. When the proportions are as atom to atom, an arsenite of iron is formed, which is soluble in ammonia and readily decomposed by boiling-water, and the solubility in ammonia is increased when the arsenic is in the ratio of two proportions to one of iron. When the oxide of iron is to the arsenic as three or four to one, the compound is still partially soluble in ammonia and readily decomposed by boiling water; but when the iron is further increased in quantity, as when the ratio is eight or twelve to one of arsenic, not only is all the arsenic removed from the fluid, and the precipitate insoluble in ammonia, but the iron retains the arsenic with such force that it is hardly possible to separate it even by the affusion of boiling-water.

From all these experiments I draw the following conclusions.

That the hydrated oxide of iron is a real chemical antidote to arsenious acid, and that when it removes arsenic from solution and soluble combinations it acts by chemically uniting with it.

That it appears much better fitted for removing arsenic, when it has been precipitated by ammonia than when precipitated by potash; and that it answers better when in the state of a moist magma, than when dried at 180°, even though, when thus dried, it still retains a considerable per centage of combined water.

That thus there appear to be good grounds for believing that in the experiments on animals, and the cases in the human subject, in which it has been found to arrest the action of the poison, that it acted as a chemical antidote and not as a mechanical protection to the stomach; that the large quantities which have been found necessary are required not to protect the stomach mechanically, but to render the poison chemically inert. That, as far as chemical evidence goes, atleast twelve parts of oxide prepared by ammonia and moist are required for each part of arsenic,* and that when the oxide has either been precipitated by potash, or been dried even at a low temperature, that about three or four times larger quantities are requisite.

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* This proportion of twelve parts of the moist ammoniacal oxide to each part of arsenic is that which has been indicated by several of the French experimentalists as being required to insure its antidotal effects.

I have likewise tried, though without any view to their being employed as antidotes, the hydrated oxide of lead and the hydrated peroxide of mercury, but with neither could I succeed in removing arsenic from its solution. Neither was there any arsenic removed from its solution by charcoal, which in fine powder has been used as a mechanical antidote to the poison.

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